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Original Article

Correlating Serum Beta hCG Levels with Transvaginal Sonographic Features of Ectopic Pregnancy

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Abstract

Background: To correlate Beta Hcg Levels with transvaginal sonographic features of ectopic pregnancy

Methods: In this prospective study 204 patients with confirmed diagnosis of ectopic pregnancy (EP), by both trasnvaginal sonography (TVS) and histopathology were included . Results of TVS and serum βHCG levels were obtained. Other variables were age, gestational age, size, site and volume of EP, fetal cardiac activity and presence or absence of pelvic ascites.

Results: Sensitivity and specificity of TVS for detection of EP was 98% and 87.5% respectively. The values of median and range for the age, gestational age, βHCG and volume of EP were 29 (17-43) years, 5(4-6) weeks, 3248.5 (14-53048) IU/L, 8648.36 (268-80491) mm^3 respectively. Most common site of EP was adnexa (93.6%) and most common side was right (52%). Fetal cardiac activity was evident in 4.4% cases and pelvic ascites was present in 64.7% cases. There was no significant difference between two βHCG groups (<2000, >2000) in terms of qualitative and quantitative variables except the volume of EP which was significantly different among groups (p value <0.0001).

Conclusion: Serum βHCG level alone cannot diagnose or exclude EP confidently and it is significantly correlated with the size of EP. The combination of serum βHCG and TVS provide highly accurate diagnostic information.

Key Words: Pregnancy, Ectopic, Chorionic Gonadotropin, Transvaginal ultrasonography.

Introduction

One of the most challenging problems in gynecology has been the early identification of EP. Early diagnosis of EP goes in more favor of conservative management. TVS and serum beta human chorionic gonadotropin (βHCG) are fundamental non-invasive modalities for detection and exclusion of EP. To some extent they both complement each other in this regard. Histopathology of the specimen is confirmatoryIn the United States, EP is estimated to occur in 1-2% of all pregnancies and accounts for 3-4% of all pregnancy-related deaths.[1] In the UK, EP remains the leading cause of pregnancy-related first trimester death (0.35 per 1000 cases of EP). In the developing world 10% of women admitted to hospital with a diagnosis of EP, ultimately die from this condition.[2]

During the 1980s and early 1990s the non-invasive methods were introduced to detect EP, like beta subunit of human chorionic gonadotropin (βHCG) and ultrasonography (USG) .[3, 4] Later on, refinement of these modalities like development of rapid essays for βHCG and high frequency transabdominal and transvaginal sonography (TVS) produced comparable detection rates as compared to laparoscopy.[5] In EP urine pregnancy test may confuse the clinicians and some suggested ultrasensitive urine test to minimize this confusion but quantitative measurement of serum βHCG proved much superior to it. [6-8] EP has lesser βHCG levels than normal intrauterine pregnancy.[9] The threshold level of βHCG to detect normal or ectopic gestation is debatable. The concept of a 'discriminatory βBCG level' was introduced in 1985 to highlight the serum βHCG level when a pregnancy should be visible on an USG.[2] The range in various studies is highly variable i.e. from 1000 to 6500 IU/L.[10-12] Due to these advances the EP related mortality ratio declined by 56.6%, from 1.15 to 0.50 deaths per 100,000 live births between 1980 to 1984 and 2003 to 2007in United States.[13]

The main focus of TVS to exclude EP relies on the detection of intrauterine gestational sac. The high frequency TVS can provide more diagnostic information about location of EP as compared to transabdominal USG. In most of the studies the main focus has been on role of TVS along with discriminatory zones of βHCG for diagnosis of EP.[14] The combination of βHCG and USG still remains the best among non-invasive diagnostic modalities.[15] The early detection of EP goes more in the favor of successful medical management.[3] The purpose of this

study was to correlate and compare the serum βHCG levels with various sonographic features of ectopic gestation and to find out whether we can rely solely on serum βHCG.

Patients and Methods

This prospective study was conducted in Dallah Hospital, Riyadh from January 2013 to October 2016, with close collaboration between departments of Obstetrics and Gynecology, Medical imaging and Pathology. Only the patients who had confirmation of EP via both TVS and HP were included in the study and serum βHCG levels were obtained. The patients, in which the duration between TVS and βHCG sample collection was more than 12 hours, were excluded. The titer of βHCG was measured with Amerlite, HCG-60 assay. TVS was performed with 6.5 MHz transducer C10-3 and transducer R1C5-9-D. The probe had angle variation from 30 to 180 degrees. Sonologist was kept ignorant of βHCG levels. The EP was defined as adnexal mass, gestational sac or embryo with or without cardiac activity outside the uterus, in the absence of intrauterine pregnancy. The various features of EP like site, size and presence or absence of fluid in the cul-de-sac were also recorded. All patients were treated according to standard hospital protocols. The samples of EP were obtained laparoscopically or via open surgical procedures during the surgical management and were sent for HP.

The quantitative variables were age of patient (in years), gestational age (in weeks), serum βHCG (in IU/L) and the volume of EP (3/4×length/2× width/2×width/2×π in mm^3, assuming shape of EP as regular ellipsoid). None of the quantitative variable shows normal distribution as assessed by Shapiro-Wilk test for normality (p value <0.0001). These variables are expressed by median, interquartile range (IQR) and range. The qualitative variables are site of EP, side of EP, presence or absence of fetal cardiac activity and fluid in cul-de-sac. These variables are expressed as frequencies and percentages. The βHCG levels were categorized into two groups (<2000 and > 2000 IU/L, loosely based on βHCG level of 2000 IU/L was considered as the threshold of the Discriminatory Zone) and both groups were compared in terms of rest of quantitative and qualitative variables by independent samples Mann–Whitney U test and Chi square tests. Non parametric correlation (Kendall's tau b) between βHCG, gestational age and volume of EP was calculated. P value of < 0.05 was considered significant.

Results

In this study, initially a total of 211 patients were included based on the TVS findings. Later on HP excluded 7 cases and our final sample was 204 patients after fulfilling the inclusion and exclusion criteria. Sensitivity, specificity, positive and negative predictive values of TVS for detection of EP was 98%, 87.5%, 99.51% and 63.64% respectively. Majority were in age group 25-35 years (Table 1). Majorty had gestational age less than 5 weeks (Table 2).The median (IQR, Range) for the age was 29.00 (10, 17-43) years and gestational age was 5.00 (1, 4-6) weeks (Table 1. Figure 1 and II show the age and gestational age distribution of patients. Serum βHCG levels were 3248.50 (12762, 14-53048) IU/L and volumes of EP were 8648.36 (13708, 268-80491) mm^3. We had 13 cases in which βHCG levels were below 100 and in five patients levels were below 50 IU/L. Putting cutoff value of 2000 IU/L, we got 120 cases (58.8 %) with serum βHCG levels > 2000 IU/L. The most common observed site for the EP was adnexa (n= 191, 93.6%) followed by ovaries (n= 10, 4.9%), scar of previous caesarian section (n= 5, 1%) and cervix (n= 1, 0.5%).

Table 1: Ectopic Pregnancy- Age Distribution

Age Group (years)	No(%)
< 25	61(29.90)
25-35	101(49.50)
> 35	42920.58)

Table 2. Gestational age

Gestational age(weeks)	No(%)
<5	128(63)
>5	76(37)

Table 3.Comparison of qualitative variables

Parameter		βHCG levels (IU/L)		Pearson Chi square	p-value
		< 2000	>2000		
Side of EP	Right	48	58	3.260	0.20
	Left	36	59		
Site of EP	Adnexal	59	132	3.813	0.051
	Non adnexal	2	11		
Fetal cardiac activity	Yes	1	8	3.514	0.061
	No	83	112		
Pelvic ascites	Yes	54	78	0.011	0.92
	No	30	42		

A total of 106 cases (52%) of EP noted on right side, 95 cases (46.6%) were found on left side while 2 cases in

scar area and one case in cervix. Fluid in the cul-de-sac was present in 132 patients (64.7%). Out of 204 EPs, TVS detected fetal cardiac activity in 9 cases (4.4%).The qualitative and quantitative variables were compared among the groups (based on βHCG levels of less or more than 2000 IU/L) (Table 3&4). The βHCG levels were significantly correlated with EP volume (tau b = 0.252, p value <0.0001, n = 204) but these were not correlated significantly with the gestational age (tau b = -0.042, p value = 0.423, n = 204).

Table 4: Comparison of quantitative variable

Parameter	βHCG levels (IU/L)		p- value
	< 2000	>2000	
	Median (IQR, range)	Median (IQR, range)	
Age (years)	28.50 (10, 18-43)	30.00 (11, 17-43)	0.94
Gestational age (weeks)	5.00 (0, 4-6)	5.00 (2, 4-6)	0.75
EP volume (mm^3)	4089.17 (8299, 359-60048)	10939.24 (12471, 268-80491)	<0.0001

Discussion

TVS is now considered to play important role in both normal and abnormal gestation. This imaging technique can be performed in the outpatient clinic or emergency department and has been reported to have a sensitivity of 90% and a specificity of 99.8%, with positive and negative predictive values of 93% and 99.8% respectively for the diagnosis of EP. [16] These findings vary a little from ours in the specificity and negative predictive values. TVS should identify the normal intrauterine gestation sac with almost 100% accuracy at a gestational age of 5.5 weeks.[2]The close correlation between serum βHCG and gestational sac size has important implication when the gestational sac is not visible inside the uterus and sonographic details are inconclusive.[14] In our study the gestational age was not correlated with the βHCG levels which is contrary to many studies.[3, 16] EP volume was significantly correlated with serum βHCG level (p value <0.0001). This correlation showed that 25% of the ranks were concordant. In 1982, Ackerman et al. showed that size of EP is correlated with βHCG levels and these findings have been evident in other studies also. [14,17-19]

We divided the βHCG levels into two categories, keeping 2000 IU/L as dividing line. This was based on the fact that βHCG level more than 2000 IU/L 95.2% specific for the diagnosis of EP.[16] Level of βHCG level < 10 IU/L has been reported in EP.[20] No single level of βHCG is diagnostic of EP and serial measurements are better predictor of the EP and its course.[21]. So it is very difficult to ascertain the threshold of βHCG for the detection of EP. We found 2 cases with 13 and 14 IU/L who had positive sonographic evidence of EP.

In our study we found that 64.7% patients had pelvic fluid detected by USG and previous studies showed the positive predictive value (PPV) of pelvic ascites for the detection of EP < 30%. Our study showed the fetal cardiac activity in 4.4% cases and in these cases the mean βHCG level was 14572 IU/L (range 1623 to 33847). These results were different as compared to recent research data which shows the detection of 10% cases of EP with cardiac activity which were having the mean βHCG level of 20980 IU/L (range 135-107949)[20]. In the past, the detection of fetal cardiac activity in EP has been in the range of 15 to 25%.[20, 22, 23] Our results showed the chances of fetal cardiac activity are more when the βHCG level> 2000 IU/L but this difference doesn't reach the level of significance (p value 0.061). This difference may be due to the fact that advanced gestation has more chances of positive fetal cardiac activity. Moreover, the presence of EP on right side has more dominance in patients with βHCG level >2000 IU/L and level of significance is just lacks behind the reference level of significance (p value 0.051).

Conclusion

1. The βHCG levels alone cannot confidently confirm or exclude the diagnosis of EP. Combination of serum βHCG level with TVS is the best non-invasive technique for this purpose.
2. There is a significant correlation between βHCG level and size of EP.
3. Right sided dominance with increasing βHCG levels needs further evaluation .

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